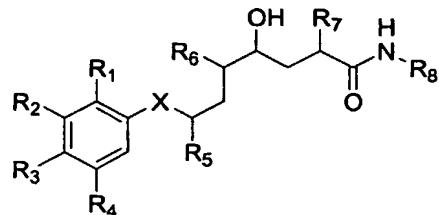


CLAIMS

We claim:

1. A method for the treatment or prevention of
 5 Alzheimer's disease, mild cognitive impairment Down's syndrome,
 Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch-
 Type, cerebral amyloid angiopathy, other degenerative dementias,
 dementias of mixed vascular and degenerative origin, dementia
 associated with Parkinson's disease, dementia associated with
 10 progressive supranuclear palsy, dementia associated with
 cortical basal degeneration, diffuse Lewy body type of
 Alzheimer's disease comprising administration of a
 therapeutically effective amount of a compound or salt of
 formula 1 to a subject in need thereof:



15 formula 1

wherein

R₁ is hydrogen, hydroxy, lower alkoxy, cycloalkoxy, lower
 alkoxylower alkoxy or free or esterified or amidated
 20 carboxylower alkoxy;
 R₂ is hydrogen, lower alkyl, cycloalkyl, lower alkoxylower
 alkyl, lower alkoxylower alkoxylower alkyl, cycloalkoxylower
 alkyl, hydroxy, optionally lower alkanoylated,
 halogenated or sulfonylated hydroxylower alkoxy; amino-
 25 lower alkyl that is unsubstituted or substituted by lower
 alkyl, by lower alkanoyl and/or by lower alkoxycarbonyl;
 optionally hydrogenated heteroaryl-lower alkyl; amino-lower
 alkoxy that is substituted by lower alkyl, by lower
 alkanoyl and/or by lower alkoxycarbonyl; oxo-lower alkoxy,

lower alkoxy, cycloalkoxy, lower alkenyloxy, cycloalkoxy-lower alkoxy, lower alkoxy-lower alkoxy, lower alkoxy-lower alkenyl, lower alkenyloxy-lower alkoxy, lower alkoxy-lower alkenyloxy, lower alkenyloxy-lower alkyl, lower alkanoyl-lower alkoxy, optionally S-oxidised lower alkylthio-lower alkoxy, lower alkylthio-(hydroxy)-lower alkoxy, aryl-lower alkoxy, optionally hydrogenated heteroaryl-lower alkoxy, cyano-lower alkoxy, free or esterified or amidated carboxy-lower alkoxy or free or esterified or amidated carboxy-lower alkyl;

R₃ is halogenated lower alkyl, lower alkoxy-lower alkyl, cycloalkoxy-lower alkyl, hydroxy-lower alkyl, optionally S-oxidised lower alkylthio-lower alkyl, optionally hydrogenated heteroarylthio-lower alkyl, optionally hydrogenated heteroaryl-lower alkyl; amino-lower alkyl that is unsubstituted or N-mono- or N,N-di-lower alkylated. N-lower alkanoylated or N-lower alkane-sulfonylated or N,N-disubstituted by lower alkylene, by unsubstituted or N'-lower alkylated or N'-lower alkanoylated aza-lower alkylene, by oxa-lower alkylene or by optionally S-oxidised thia-lower alkylene; cyano-lower alkyl, free or esterified or amidated carboxy-lower alkyl, cycloalkyl, aryl, hydroxy, lower alkoxy, cycloalkoxy, lower alkoxy-lower alkoxy, cycloalkoxy-lower alkoxy, hydroxy-lower alkoxy, aryl-lower alkoxy, optionally halogenated lower alkoxy, optionally S-oxidised lower alkylthio-lower alkoxy, optionally hydrogenated heteroaryl-lower alkoxy, optionally hydrogenated heteroarylthio-lower alkoxy; amino-lower alkoxy that is unsubstituted or N-mono- or N,N-di-lower alkylated. N-lower alkanoylated or N-lower alkanesulfonylated or substituted by lower alkylene, by unsubstituted or N'-lower alkylated or N'-lower alkanoylated aza-lower alkylene, by oxa-lower alkylene or

by optionally S-oxidised thia-lower alkylene; cyano-lower alkoxy or free or esterified or amidated carboxy-lower alkoxy;

R₄ is hydrogen, lower alkyl, hydroxy, lower alkoxy or
5 cycloalkoxy;

X is methylene;

R₅ is lower alkyl or cycloalkyl;

R₆ is unsubstituted or N-mono- or N,N-di-lower alkylated or N-lower alkanoylated amino;

10 R₇ is lower alkyl, lower alkenyl, cycloalkyl or aryl-lower alkyl; and

R₈ is lower alkyl, cycloalkyl, free or aliphatically esterified or etherified hydroxy-lower alkyl; amino-lower alkyl that is unsubstituted or N-lower alkanoylated or N-mono- or N,N-di-lower alkylated or N,N-disubstituted by lower alkylene, by hydroxy-lower alkoxy- or lower alkanoyloxy-lower alkylene, by unsubstituted or N'-lower alkanoylated or N'-lower alkylated aza-lower alkylene, by oxa-lower alkylene or by optionally S-oxidised thia-lower alkylene; free or esterified or amidated carboxy-lower alkyl, free or esterified or amidated dicarboxy-lower alkyl, free or esterified or amidated carboxycycloalkyl-lower alkyl, cyano-lower alkyl, lower alkanesulfonyl-lower alkyl, unsubstituted or N-mono- or N,N-di-lower alkylated thiocarbamoyl-lower alkyl, unsubstituted or N-mono- or N,N-di-lower alkylated sulfamoyl-lower alkyl, or a heteroaryl radical bonded via a carbon atom and optionally hydrogenated and/or oxo-substituted, or lower alkyl substituted by a heteroaryl radical bonded via a carbon atom and optionally hydrogenated and/or oxo-substituted, or a pharmaceutically acceptable salt thereof. .

2. A method according to claim 1 wherein

R₁ is hydrogen, hydroxy, lower alkoxy, cycloalkoxy, lower alkoxy-lower alkoxy, carboxy-lower alkoxy, lower alkoxy carbonyl-lower alkoxy, carbamoyl-lower alkoxy or N-

5 mono- or N,N-di-lower alkylcarbamoyl-lower alkoxy;

R₂ is hydrogen, lower alkyl, cycloalkyl, lower alkoxy-lower alkyl, lower alkoxy-lower alkoxy-lower alkyl, cycloalkoxy-lower alkyl, hydroxy, lower alkanoyloxy-lower alkyl, hydroxy-lower alkoxy, halo-(hydroxy)-lower alkoxy, lower

10 alkane-sulfonyl-(hydroxy)-lower alkoxy, amino-lower alkyl, lower alkylamino-lower alkyl, di-lower alkylamino-lower alkyl, lower alkanoylamino-lower alkyl, lower alkoxycarbonylamino-lower alkyl, amino-lower alkoxy, lower

15 alkylamino-lower alkoxy, di-lower alkylamino-lower alkoxy, lower alkanoylamino-lower alkoxy, lower alkoxycarbonylamino-lower alkoxy, oxo-lower alkoxy, lower

alkoxy, cycloalkoxy, lower alkenyloxy, cycloalkoxy-lower alkoxy, lower alkoxy-lower alkoxy, lower alkoxy-lower alkenyl, lower alkenyloxy-lower alkoxy, lower alkoxy-lower

20 alkenyloxy, lower alkenyloxy-lower alkyl, lower alkanoyl-lower alkoxy, lower alkylthio-lower alkoxy, lower alkanesulfonyl-lower alkoxy, lower alkylthio-(hydroxy)-lower alkoxy, aryl-lower alkoxy, thiazolylthio-lower alkoxy

25 or thiazolinylthio-lower alkoxy, imidazolylthio-lower alkoxy, optionally N-oxidised pyridylthio-lower alkoxy, pyrimidinylthio-lower alkoxy, cyano-lower alkoxy, lower

alkoxycarbonyl-lower alkoxy, carbamoyl-lower alkoxy, N-mono- or N, N-all-lower alkylcarbamoyl-lower alkoxy, carboxy-lower alkyl, lower alkoxy-carbonyl-lower alkyl,

30 carbamoyl-lower alkyl or N-mono- or N,N-di-lower alkyl-carbamoyl-lower alkyl;

R₃ is lower alkyl, polyhalo-lower alkyl, lower alkoxy-lower alkyl, cycloalkoxy-lower alkyl, hydroxy-lower alkyl, lower

alkylthio-lower alkyl, lower alkanesulfonyl-lower alkyl, optionally partially hydrogenated or N-oxidised pyridyl-lower alkyl, thiazolylthio-lower alkyl or thiazolinylthio-lower alkyl, imidazolylthio-lower alkyl, optionally N-
5 oxidised pyridylthio-lower alkyl, pyrimidinylthio-lower alkyl, amine-lower alkyl, lower alkylamino-lower alkyl, di-lower alkylamino-lower alkyl, lower alkanoylamino-lower alkyl, lower alkanesulfonylamino-lower alkyl, polyhalo-lower
10 alkanesulfonylamino-lower alkyl, pyrrolidino-lower alkyl, piperidino-lower alkyl, piperazino-, N'-lower alkylpiperazino- or N'-lower alkanoylpiperazino-lower alkyl, morpholino-lower alkyl, thiomorpholino-. S-oxothiomorpholino- or S,S-dioxothiomorpholino-lower alkyl, cyano-lower alkyl, carboxy-lower alkyl, lower
15 alkoxycarbonyl-lower alkyl, carbamoyl-lower alkyl, N-mono- or N,N-di-lower alkylcarbamoyl-lower alkyl, cycloalkyl; phenyl or naphthyl that is unsubstituted or mono-, di- or tri-substituted by lower alkyl, lower alkoxy, hydroxy, lower alkylamino, di-lower alkylamino, halogen and/or by trifluoromethyl; hydroxy, lower alkoxy, cycloalkoxy, lower
20 alkoxy-lower alkoxy, cycloalkoxy-lower alkoxy, hydroxy-lower alkoxy; phenyl-lower alkoxy or naphthyl-lower alkoxy that is unsubstituted or mono-, di- or tri-substituted by lower alkyl, lower alkoxy, hydroxy, lower alkylamino, di-lower
25 alkylamino, halogen and/or by trifluoromethyl; lower alkoxy, polyhalo-lower alkoxy, lower alkylthio-lower alkoxy, lower alkanesulfonyl-lower alkoxy, optionally partially hydrogenated heteroaryl-lower alkoxy, optionally partially or fully hydrogenated hetero-arylthio-lower alkoxy, such as thiazolylthio-lower alkoxy or thiazolinylthio-lower alkoxy, imidazolylthio-lower alkoxy, optionally N-oxidised
30 pyridylthio-lower alkoxy, pyrimidinylthio-lower alkoxy, amine-lower alkoxy, lower alkylamino-lower alkoxy, di-lower

alkylamino-lower alkoxy, lower alkanoylamino-lower alkoxy, lower alkanesulfonylamino-lower alkoxy, polyhalo-lower alkanesulfonylamino-lower alkoxy, pyrrolidino-lower alkoxy, piperidino-lower alkoxy, piperazino-, N'-lower alkylpiperazino- or N'-lower alkanoylpiperazino-lower alkoxy, morpholino-lower alkoxy, thiomorpholino-, S-oxothiomorpholino- or S,S-dioxothiomorpholino-lower alkoxy, cyano-lower alkoxy, carboxy-lower alkoxy, lower alkoxy carbonyl-lower alkoxy, carbamoyl-lower alkoxy or N-mono- or N,N-di-lower alkylcarbamoyl-lower alkoxy;

5 R₄ is hydrogen, lower alkyl, hydroxy, lower alkoxy or cycloalkoxy;

X is methylene;

R₅ is lower alkyl or cycloalkyl;

15 R₆ is amino, lower alkylamino, di-lower alkylamino or lower alkanoylamino;

R₇ is lower alkyl, lower alkenyl, cycloalkyl, or phenyl- or naphthyl-lower alkyl that is unsubstituted or mono-, di- or tri-substituted by lower alkyl, lower alkoxy, hydroxy, lower alkylamino, di-lower alkylamino, halogen and/or by trifluoromethyl; and

20 R₈ is lower alkyl, cycloalkyl, hydroxy-lower alkyl, lower alkanoyloxy-lower alkyl, lower alkoxy-lower alkyl or lower alkenyloxy-lower alkyl, amino-lower alkyl, lower alkanoylamino-lower alkyl. N-mono- or N,N-di-lower alkylamino-lower alkyl, optionally hydroxylated or lower alkoxylated piperidino-lower alkyl, such as piperidino-lower alkyl, hydroxypiperidino-lower alkyl or lower alkoxy-piperidino-lower alkyl, piperazino-, N'-lower alkylpiperazino- or N'-lower alkanoylpiperazino-lower alkyl, unsubstituted or lower alkylated morpholino-lower alkyl, such as morpholino-lower alkyl or dimethylmorpholino-lower alkyl, or optionally S-oxidised

thiomorpholino-lower alkyl, such as thiomorpholino-lower alkyl, S,S-dioxothiomorpholino-lower alkyl, carboxy-lower alkyl, lower alkoxy carbonyl-lower alkyl, carbamoyl-lower alkyl, N-mono- or N,N-di-lower alkylcarbamoyl-lower alkyl,
5 dicarboxy-lower alkyl, di-lower alkoxy carbonyl-lower alkyl, dicarbamoyl-lower alkyl, di-(N-mono- or N,N-di-lower alkylcarbamoyl)-lower alkyl, carboxy-(hydroxy)-lower alkyl, lower alkoxy-carbonyl-(hydroxy)-lower alkyl or carbamoyl-(hydroxy)-lower alkyl, cyano-lower alkyl, lower
10 alkanesulfonyl-lower alkyl, sulfamoyl-lower alkyl, lower alkyl-sulfamoyl-lower alkyl, di-lower alkylsulfamoyl-lower alkyl, thiocarbamoyl-lower alkyl, lower alkylthiocarbamoyl-lower alkyl, di-lower alkylthiocarbamoyl-lower alkyl, pyrrolidinyl, imidazolyl, benzimidazolyl, oxadiazolyl,
15 pyridyl, oxopiperidinyl, quinolinyl, unsubstituted or N-lower alkanoylated piperidyl or pyrrolidinyl, imidazolyl-lower alkyl, benzimidazolyl-lower alkyl, oxadiazolyl-lower alkyl, pyridyl-lower alkyl, unsubstituted or N-lower alkanoylated piperidyl-lower alkyl or pyrrolidinyl-lower
20 alkyl, oxopiperidinyl-lower alkyl, quinolinyl-lower alkyl, morpholinocarbonyl-lower alkyl or unsubstituted or N-lower alkanoylated piperidyl-lower alkyl, or a pharmaceutically acceptable salt thereof. .

25 3. A method according to claim 1 wherein

R₁ is hydrogen;

R₂ is lower alkyl, lower alkoxy-lower alkyl, lower alkoxy-lower alkoxy, lower alkoxy-tower alkoxy-lower alkyl; phenyl-lower alkoxy that is unsubstituted or substituted by bower alkyl, lower alkoxy, hydroxy, halogen, nitro and/or by amino; optionally N-oxidised pyridyl-lower alkoxy, lower alkylthio-lower alkoxy, lower alkanesulfonyl-lower alkoxy, lower alkanoyl-lower alkoxy, optionally N-oxidised pyridyl-

lower alkoxy, cyano-lower alkoxy, carboxy-lower alkoxy,
lower alkoxycarbonyl-lower alkoxy, carbamoyl-lower alkoxy,
lower alkylcarbamoyl-lower alkoxy or di-lower
alkylcarbamoyl-lower alkoxy,

5 R₃ is hydrogen, lower alkyl, hydroxy, lower alkoxy or polyhalo-lower alkoxy,

R₄ is hydrogen or together with R₃ is lower alkylidenedioxy,
X is methylene,

R₅ is lower alkyl or cycloalkyl;

10 R₆ is amine, lower alkylamino, di-lower alkylamino or lower alkanoylamino,

R₇ is lower alkyl, and

R₈ is lower alkyl, hydroxy-lower alkyl, lower alkanoyl-lower alkyl, lower alkoxy-lower alkyl, lower alkenyloxy-lower

15 alkyl, amino-lower alkyl, lower alkanoyl-amino-lower alkyl, such as 2-(C₁-C₄ alkanoylamino)-2-methyl-propyl, such as 2-acetylaminoo-2-methyl-propyl or 2-formylamino-2-methyl-propyl, N-mono- or N,N-di-lower alkylamino-lower alkyl, piperidino-lower alkyl, hydroxypiperidino-lower alkyl,

20 lower alkoxypiperidino-lower alkyl, morpholino-lower alkyl, dimethylmorpholino-lower alkyl, thiomorpholino-lower alkyl.

S,S-dioxothiomorpholino-lower alkyl, Carboxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, carbamoyl-lower alkyl, N-mono- or N,N-di-lower alkylcarbamoyl-lower alkyl, carboxy-

25 (hydroxy)-lower alkyl, lower alkoxycarbonyl-(hydroxy)-lower alkyl, carbamoyl-(hydroxy)-lower alkyl, 5- or 6-membered carboxycycloalkyl-lower alkyl, 5- or 6-membered lower alkoxycarbonylcycloalkyl-lower alkyl. 5- or 6-membered carbamoylcycloalkyl-lower alkyl, 5- or 6-membered N-mono-

30 or N, N-di-lower alkylcarbamoylcycloalkyl-lower alkyl, cyano-lower alkyl, lower alkanesulfonyl-lower alkyl, sulfamoyl-lower alkyl, lower alkylsulfamoyl-lower alkyl or di-lower alkylsulfamoyl-lower alkyl, imidazolyl-lower

alkyl, oxopyrrolidinyl-lower alkyl, benzimidazolyl-lower alkyl, oxadiazolyl-lower alkyl, pyridyl-lower alkyl, oxopiperidinyl-lower alkyl or quinolinyl-lower alkyl, piperidin-4-yl-lower alkyl or 1-C₁-C₇-lower alkanoylpiperidin-4-yl-lower alkyl, or a pharmaceutically acceptable salt thereof. .

4. A method according to claim 1 wherein

R₁ and R₄ are hydrogen;

10 R₂ is C₁-C₄ alkoxy- C₁-C₄ alkoxy or C₁-C₄ alkoxy- C₁-C₄ alkyl;

R₃ is C₁-C₄ alkyl or C₁-C₄ alkoxy;

R₆ is amino;

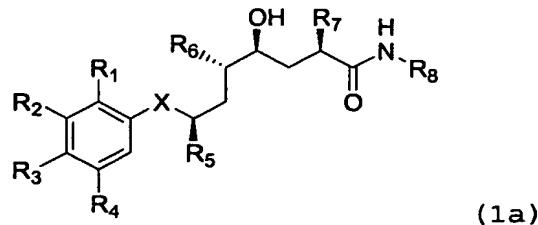
X is methylene;

R₅ and R₇ are branched C₁-C₄ alkyl; and

15 R₈ is carbamoyl- C₁-C₄ alkyl, N-C₁-C₄ alkylcarbamoyl- C₁-C₄ alkyl, N,N-di- C₁-C₄ alkyl-carbamoyl- C₁-C₄ alkyl, morpholino- C₁-C₄ alkyl, thiomorpholino- C₁-C₄ alkyl, 4-(1- C₁-C₄ alkanoylpiperidyl)- C₁-C₄ alkyl or 2-oxopyrrolidinyl- C₁-C₄ alkyl, or a pharmaceutically acceptable salt thereof. .

20

5. A method according to claim 1 wherein at least one asymmetric carbon atom of the main chain has the stereochemical configuration shown in formula 1a



25 each of the variables being as defined in claim 1, or a pharmaceutically acceptable salt thereof.

6. A method according to claim 1 wherein the compound is selected from the group consisting of:

2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- (p-tert-butyl-phenyl)-octanoic acid (N-butyl)amide;

2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -ethyl-8- (p-tert-butyl-phenyl)-octanoic acid (N-butyl)amide;

5 2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -methyl-8- (4-biphenyl-octanoic acid (N-butyl)amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amine-7 (S) -isopropyl-8- (3-hydroxy-4-tert-butyl-phenyl)-octanoic acid (N-butyl)amide;

10 2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- (2-hydroxy-4-tert-butyl-phenyl)-octanoic acid (N-butyl)amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- (3-ethoxycarbonylmethoxy-4-tert-butyl-phenyl)-octanoic acid (N-butyl)amide;

15 2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- (3-allyloxy-4-tert-butyl-phenyl)-octanoic acid (N-butyl)amide;

2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- (3-methoxycarbonyl-allyloxy-4-tert-butyl-phenyl)-octanoic acid (N-butyl)amide;

20 2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- (3-methoxycarbonyl-methoxy-4-tert-butyl-phenyl)-octanoic acid (N-butyl)amide;

2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- (3-carbamoyl-methoxy-4-tert-butyl-phenyl)-octanoic acid (N-butyl)amide;

25 2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-(pyrid-2-yl-methoxy)-4-tert-butyl-phenyl]-octanoic acid (N-butyl)amide;

2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-(pyrid-4-yl-methoxy)-4-tert-butyl-phenyl]-octanoic acid (N-butyl)amide;

30 2 (R,S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-(N-oxido-pyrid-2-yl-methoxy)-4-tert-butyl-phenyl]-octanoic acid (N-butyl)amide;

2 (R, S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
5 (2-ethoxycarbonylallyl-oxy)-4-tert-butyl-phenyl]-octanoic acid
(N-butyl) amide;

2 (R, S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
10 (2-ethoxycarbonyl-propyloxy)-4-tert-butyl-phenyl]-octanoic acid
(N-butyl) amide;

2 (R, S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
15 (methylthio-methoxy)-4-tert-butyl-phenyl]-octanoic acid (N-
butyl) amide;

2 (R, S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
20 (methylsulfonyl-methoxy)-4-tert-butyl-phenyl]-octanoic acid (N-
butyl) amide;

2 (R, S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
25 (carboxy-methoxy)-4-tert-butyl-phenyl]-octanoic acid (N-
butyl) amide;

2 (R, S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
30 (3, 3-dimethyl-2-oxo-butyloxy)-4-tert-butyl-phenyl]-octanoic acid
(N-butyl) amide;

2 (R, S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
35 (2-nitrobenzyloxy)-4-tert-butyl-phenyl]-octanoic acid (N-
butyl) amide;

2 (R, S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
40 (2-aminobenzyloxy)-4-tert-butyl-phenyl]-octanoic acid (N-
butyl) amide;

2 (R, S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
45 (3-chloro-2 (R) hydroxypropyloxy)-4-tert-butyl-phenyl]-octanoic
acid (N-butyl) amide;

2 (R, S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
50 (3-methylthio-2 (S, R) -hydroxypropyloxy)-4-tert-butyl-phenyl]-
octanoic acid (N-butyl) amide;

2 (R, S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
55 (3-methylsulfonyl- (S, R) -hydroxypropyloxy)-4-tert-butyl-phenyl]-
octanoic acid (N-butyl) amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
(methyldisulfonyl-methoxy)-4-tert-butyl-phenyl]-octanoic acid (N-
3-morpholino-propyl) amide;

5 2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
methoxycarbonyl-methoxy-phenyl]-octanoic acid (N-butyl) amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
(methoxycarbonyl-methoxy)-4-methoxy-phenyl]-octanoic acid (N-
butyl) amide;

10 2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3- (N-
methyl-carbamoyl-methoxy)-4-methoxy-phenyl]-octanoic acid (N-
butyl) amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3- (3-
methyldisulfonyl-propyloxy)-4-methoxy-phenyl]-octanoic acid (N-
butyl) amide;

15 2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
(methyldisulfonyl-methoxy)-4-methoxy-phenyl]-octanoic acid (N-
butyl) amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3- (3-
methoxy-propyloxy)-4-methoxy-phenyl]-octanoic acid (N-
butyl) amide;

20 2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3- (2-
methoxy-ethoxy)-4-methoxy-phenyl]-octanoic acid (N-butyl) amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3- (3-
hydroxy-propyloxy)-4-methoxy-phenyl]-octanoic acid (N-
butyl) amide;

25 2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
(carbamoylmethoxy)-4-methoxy-phenyl]-octanoic acid (N-
butyl) amide;

30 2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3-
cyanomethoxy-4-methoxy-phenyl]-octanoic acid (N-butyl) amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8- [3- (4-
methoxy-butoxy)-4-methoxy-phenyl]-octanoic acid (N-butyl) amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8-[3-(2-ethoxy-ethoxy)-4-methoxy-phenyl]-octanoic acid (N-butyl) amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8-[3-[2-(2-methoxy-ethoxy)-ethoxy]-4-methoxy-phenyl]-octanoic acid (N-
5 butyl) amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8-(3-pentyloxy-4-methoxy-phenyl)-octanoic acid (N-butyl) amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8-(3-benzyloxy-4-methoxy-phenyl)-octanoic acid (N-butyl) amide;

10 2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8-[3-(3-ethoxy-propyloxy)-4methoxy-phenyl]-octanoic acid (N-butyl) amide;

2 (R) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8-[3-(pyrid-4-ylmethoxy)-4-methoxy-phenyl]-octanoic acid (N-butyl) amide;

15 2 (R, S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8-(2-ethoxycarbonyl-methoxy-4-tert-butyl-phenyl)-octanoic acid (N-butyl) amide;

2 (R, S) -methyl-4 (S) -hydroxy-5 (S) -amino-7 (S) -isopropyl-8-(2-ethoxycarbonyl-4-tert-butyl-phenyl)-octanoic acid (N-
20 butyl) amide;

5 (S) -amino-4 (S) -hydroxy-2 (S), 7 (S) -diisopropyl-8-[4-(3-hydroxypropyloxy)-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(2-carbamoyl-2,2-dimethyl-ethyl)]-amide;

25 5 (S) -amino-4 (S) -hydroxy-2 (S), 7 (S) -diisopropyl-8-[4-isopropyl-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(2-carbamoyl-2,2-dimethyl-ethyl)]-amide;

5 (S) -amino-4 (S) -hydroxy-2 (S), 7 (S) -diisopropyl-8-[4-tert-butyl-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(2-carbamoyl-2,2-dimethyl-ethyl)]-amide;

30 5 (S) -amino-4 (S) -hydroxy-2 (S), 7 (S) -diisopropyl-8-[4-(3-methylsulfonyl-propyloxy)-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid (N-2-morpholinoethyl) amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-(3-methylsulfonyl-propyloxy)-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(2-carbamoyl-2,2-dimethyl-ethyl)]-amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[3,4-di(3-hydroxypropyloxy)-phenyl]-octanoic acid (N-2-morpholinoethyl) amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[3,4-di(3-hydroxypropyloxy)-phenyl]-octanoic acid [N-(2-carbamoyl-2,2-dimethyl-ethyl)]-amide;

10 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-(3-N-methylcarbamoyl-propyl)-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid (N-2-morpholinoethyl) amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-(2-morpholinoethoxy)-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(2-carbamoyl-2,2-dimethyl-ethyl)]-amide;

15 [5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[3-(3-methoxypropyloxy)-4,5-ethylenedioxy-phenyl]-octanoic acid (N-2-morpholinoethyl) amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[3-(3-methoxypropyloxy)-4,5-ethylenedioxy-phenyl]-octanoic acid [N-(2-carbamoyl-2,2-dimethyl-ethyl)]-amide;

20 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[3-(3-methoxy-propyloxy)-4,5-methylenedioxy-phenyl]-octanoic acid (N-2-morpholinoethyl) amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[3-(3-methoxy-propyloxy)-4,5-methylenedioxy-phenyl]-octanoic acid (N-2-morpholinoethyl) amide;

25 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[3-(3-methoxypropyloxy)-4,5-methylenedioxy-phenyl]-octanoic acid [N-(2-carbamoyl-2,2-dimethyl-ethyl)] amide;]

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(2-carbamoyl-2,2-ethylene-ethyl)]-amide;

30 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propoxy)-phenyl]-octanoic acid [N-(3(S)-2-oxo-pyrrolidin-3-yl-methyl)] amide;

5 (S)-amino-4(S)-hydroxy-7(S)-isopropyl-2(R)-methyl-8-[4-methoxy-3-(4-methoxy-but-2-eneoxy)-phenyl]-octanoic acid (N-butyl)amide;

5 (S)-amino-4(S)-hydroxy-7(S)-isopropyl-2(R)-methyl-8-[4-hydroxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid (N-butyl)amide;

10 5 (S)-amino-4(S)-hydroxy-7(S)-isopropyl-2(R)-methyl-8-H-benzyloxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid (N-butyl)amide;

15 5 (S)-amino-4(S)-hydroxy-7(S)-isopropyl-2(R)-methyl-8-[4-(2,2,2-trifluoroethoxy)-3-(3-methoxypropyloxy)-phenyl]-octanoic acid (N-butyl)amide;

20 5 (S)-amino-4(S)-hydroxy-7(S)-isopropyl-2(R)-methyl-8-[4-(3-hydroxy-propyloxy)-3-(3-methoxypropyloxy)-phenyl]-octanoic acid (N-butyl)amide;

25 5 (S)-amino-4(S)-hydroxy-7(S)-isopropyl-2(R)-methyl-8-[4-(2-amino-ethoxy)-3-(3-methoxypropyloxy)-phenyl]-octanoic acid (N-butyl)amide;

30 5 (S)-amino-4(S)-hydroxy-7(S)-isopropyl-2(R)-methyl-8-[4-(5-amino-pentyloxy)-3-(3-methoxypropyloxy)-phenyl]-octanoic acid (N-butyl)amide;

5 (S)-amino-4(S)-hydroxy-7(S)-isopropyl-2(R)-methyl-8-[4-(4-amino-butyloxy)-3-(3-methoxypropyloxy)-phenyl]-octanoic acid (N-butyl)amide;

5 (S)-amino-4(S)-hydroxy-7(S)-isopropyl-2(R)-methyl-8-[4-(4-N,N-dimethylamino-butyloxy)-3-(3-methoxypropyloxy)-phenyl]-octanoic acid (N-butyl)amide;

35 5 (S)-amino-4(S)-hydroxy-7(S)-isopropyl-2(R)-methyl-8-{4-[4-N-(trifluoromethane-sulfonylaminobutyloxy)-3-(3-methoxypropyloxy)-phenyl]}-octanoic acid (N-butyl)-amide;

5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-carboxymethoxy-3-(3-methoxypropyloxy)-phenyl]-octanoic acid (N-butyl) amide;

5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-(3-ethoxycarbonyl-propyloxy)-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid (N-butyl) amide;

10 5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-(3-carboxy-propyloxy)-3-(3-methoxypropyloxy)-phenyl]-octanoic acid (N-butyl) amide;

15 5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-(4-methoxycarbonylbutyloxy)-3-(3-methoxypropyloxy)-phenyl]-octanoic acid (N-butyl) amide;

20 5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-(4-carboxy-butyloxy)-3-(3-methoxypropyloxy)-phenyl]-octanoic acid (N-butyl) amide;

25 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid (N-butyl) amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(2-methoxymethoxy-ethyl)-phenyl]-octanoic acid (N-butyl) amide;

30 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-(3-hydroxypropyloxy)-3-(methoxypropyloxy)-phenyl]-octanoic acid N-(2-morpholinoethyl) amide;

35 5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-[2-(4-hydroxypiperidin-1-yl)ethyl] amide dihydrochloride;

40 5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-[2-(trans-2,6-dimethyl-morpholino)ethyl] amide;

45 5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-methoxy-3-(3-methoxypropyloxy)-phenyl]-octanoic acid N-[2-(cis-2,6-dimethyl-morpholino)ethyl] amide;

5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-(2-piperidinoethyl)amide;

5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-[2-(4-methoxypiperidino)-ethyl]amide;

10 5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-(2-thiomorpholinoethyl)amide;

15 5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(3-hydroxypropyl)]amide;

15 5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(4-acetoxybutyl)]amide;

5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(3-cyanopropyl)]amide;

20 5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(3-methoxypropyl)]amide;

5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(2-acetylaminooethyl)]amide;

25 5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid {N-[2-(2-pyridyl)-ethyl]}amide;

30 5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-[2-(N-oxomorpholino)ethyl]amide;

5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid {N-[3-(tert-butylsulfonyl)-propyl]}amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8 -[4-methoxy-3 - (3-methoxy-propyloxy) -phenyl] -octanoic acid {N- [3-(ethylsulfonyl) -propyl] } -amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8 -[4-methoxy-3 - (3-methoxy-propyloxy) -phenyl] -octanoic acid {N- [2-(ethylsulfonyl) -ethyl] } -amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8 -[4-methoxy-3 - (3-methoxy-propyloxy) -phenyl] -octanoic acid {N- [2- (N-butylsulfonyl) -ethyl] } -amide;

10 [(S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8 -[4-methoxy-3 - (3-methoxy-propyloxy) -phenyl] -octanoic acid {N- [2- (N,N-dimethylsulfonylamino) -ethyl] } -amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8 -[4-methoxy-3 - (3-methoxy-propyloxy) -phenyl] -octanoic acid {N- [3- (1H-tetrazol-5-yl) -propyl] } -amide;

15 5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8 -[4-methoxy-3 - (3-methoxy-propyloxy) -phenyl] -octanoic acid {N- [3- (1H-imidazol-5-yl) -propyl] } -amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8 -[4-methoxy-3 - (3-methoxy-propyloxy) -phenyl] -octanoic acid {N- [3- (3-methyl-1,2,4-oxadiazol-5-yl) -propyl] } -amide;

20 5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8 -[4-methoxy-3 - (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (3-aminopropyl)] -amide;

25 5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8 -[4-methoxy-3 - (3-methoxy-propyloxy) -phenyl] -octanoic acid {N- [2-dimethylamino-ethyl] } -amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8 -[4-methoxy-3 - (3-methoxy-propyloxy) -phenyl] -octanoic acid N- (2-

30 morpholinoethyl) amide;

5 (S) -amino-4 (S) -hydroxy-7 (S) -isopropyl-2 (R) -methyl-8 -[4-methoxy-3 - (3-methoxy-propyloxy) -phenyl] -octanoic acid N- (3-morpholinopropyl) amide;

5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-[2-(1,1-dioxothiomorpholino)ethyl]amide;

5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-(2-ethoxycarbonylethyl)amide;

5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(2-carboxy-ethyl)]-amide;

10 5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(3-methoxycarbonyl-ethyl)]-amide;

15 5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(3-carboxypropyl)]-amide;

5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(2-carbamoylethyl)]-amide;

20 5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(4-carbamoylbutyl)]-amide;

5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-{3-[N-(2-methoxyethyl)carbamoyl]propyl}amide;

25 5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-(4-morpholino-4-oxo-butyl)amide;

30 5 (S)-amino-4 (S)-hydroxy-7 (S)-isopropyl-2 (R)-methyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(2-carbamoyl-2,2-dimethyl-ethyl)]-amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-(1,1-dimethyl-2-morpholino-ethyl)amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-[1 (R, S)-methyl-2-morpholino-ethyl] amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(1-carbamoyl-1-methyl-ethyl)]-amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(1-carbamoyl-methyl)]-amide;

10 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(2-carbamoyl-ethyl)]-amide;

15 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-[2-(N-methyl-carbamoyl)ethyl] amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-(3-morpholino-3-oxo-propyl) amide;

20 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid {N-[2-(N, N-dimethyl-carbamoyl)-1 (R, S)-methyl-ethyl]}-amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(2-carbamoyl-1(R)-isopropyl-ethyl)]-amide;

25 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid {N-[2-(N-methylcarbamoyl)-1(R)-isopropyl-ethyl]}-amide;

30 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid {N-[2-(N,N-dimethylcarbamoyl)-1(R)-isopropyl-ethyl]}-amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(1(S)-carbamoyl-2-hydroxy-ethyl)]-amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-
3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(1(S), 2-
dicarbamoyl-ethyl)]-amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-
5 3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(1(S), 3-
dicarbamoyl-propyl)]-amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-
3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(1(S)-
carbamoyl-propyl)]-amide;

10 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-
3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(1(S)-
carbamoyl-2 (S)-methyl-butyl)]-amide;

15 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-
3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-[2(R, S)-
carbamoyl-2 (R, S)-methyl-ethyl]-amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-
3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(2-carbamoyl-
1 (S)-methyl-ethyl)]-amide;

20 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-
3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(2-carbamoyl-1
(R)-methyl-ethyl)]-amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-
3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-[2 (S)-carbamoyl-
2 (S)-methylethyl]-amide;

25 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-
3-(3-methoxy-propyloxy)-phenyl]-octanoic acid {N-[2 (S)-(N-
methyl-carbamoyl)-2 (S)-methyl-ethyl]}-amide;

30 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-
3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(2-carboxy-2, 2-
dimethyl-ethyl)]-amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-
3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(2-carboxy-2, 2-
diethyl-ethyl)]-amide;

- 5 (S)-amino-4(S)-hydroxy-2(S), 7(S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-[(1-carboxy-cyclopentyl)-methyl]amide;
- 5 (S)-amino-4(S)-hydroxy-2(S), 7(S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid {N-[2-(1H-tetrazol-5-yl)-ethyl]}-amide;
- 5 (S)-amino-4(S)-hydroxy-2(S), 7(S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-[1(S)-(5-oxopyrrolidin-2-yl)methyl]-amide;
- 10 5 (S)-amino-4(S)-hydroxy-2(S), 7(S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-[1(R)-(5-oxopyrrolidin-2-yl)methyl]-amide;
- 15 5 (S)-amine-4(S)-hydroxy-2(S), 7(S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-[N-(morpholin-4-yl)carbamoyl-methyl]amide;
- 20 5 (S)-amino-4(S)-hydroxy-2(S), 7(S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(1(S)-carbamoyl-ethyl)]-amide;
- 25 5 (S)-amino-4(S)-hydroxy-2(S), 7(S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-{1(S)-[(N-methyl)-carbamoyl]-ethyl}-amide;
- 30 5 (S)-amino-4(S)-hydroxy-2(S), 7(S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-{1(S)-[(N,N-dimethyl)-carbamoyl]-ethyl}-amide;
- 35 5 (S)-amino-4(S)-hydroxy-2(S), 7(S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-{1(S)-N-[(morpholin-4-yl)-carbamoyl]-ethyl}amide;
- 40 5 (S)-amino-4(S)-hydroxy-2(S), 7(S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-[1(S)-carbamoylbutyl]amide;
- 45 5 (S)-amino-4(S)-hydroxy-2(S), 7(S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-[1(S)-carbamoyl-2-methyl-propyl]-amide;

5 (S)-amino-4(S)-hydroxy-2(S),7(S)-diisopropyl-8-[4-methoxy-
3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-[1(S)-(N-
methylcarbamoyl)-2-methyl-propyl]amide;

5 (S)-amino-4(S)-hydroxy-2(S),7(S)-diisopropyl-8-[4-methoxy-
3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-[1(S)-(N,N-
dimethylcarbamoyl)-2-methyl-propyl]amide;

10 5 (S)-amino-4(S)-hydroxy-2(S),7(S)-diisopropyl-8-[4-methoxy-
3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-[1(S)-[N-
(morpholin-4-yl)carbamoyl]-2-methyl-propyl]amide;

15 5 (S)-amino-4(S)-hydroxy-2(S),7(S)-diisopropyl-8-[4-methoxy-
3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-[2-(N-
methylsulfonylamino)ethyl]amide;

20 5 (S)-amino-4(S)-hydroxy-2(S),7(S)-diisopropyl-8-[4-methoxy-
3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-[2-[N-
15 (morpholin-4-yl)-sulfonyl]ethyl]amide;

25 5 (S)-amino-4(S)-hydroxy-2(S),7(S)-diisopropyl-8-[4-methoxy-
3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-[(N-acetyl-
piperidin-4-yl)methyl]amide;

30 5 (S)-amino-4(S)-hydroxy-2(S),7(S)-diisopropyl-8-[4-methoxy-
3-(4-methoxy-butyl)-phenyl]-octanoic acid N-(2-carbamoyl-2,2-
dimethylethyl)amide;

35 5 (S)-amino-4(S)-hydroxy-2(S),7(S)-diisopropyl-8-[4-methoxy-
3-(3-methoxy-propyloxy)-phenyl]-octanoic acid N-[2-(N,N-
dimethylcarbamoyl)ethyl]amide;

40 5 (S)-amino-4(S)-hydroxy-2(S),7(S)-diisopropyl-8-[4-methoxy-
3-(4-methoxybutylphenyl)-octanoic acid N-(2-
morpholinoethyl)amide;

and a pharmaceutically salt thereof.

45 7. A method according to claim 1, which is selected from
the group consisting of:

- 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-
3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(3(R)-2-oxo-
pyrrolidin-3-yl-methyl)]-amide;
- 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-
5 3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(3(S)-2-oxo-
piperidin-3-yl-methyl)]-amide;
- 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-
3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(3(R)-2-oxo-
piperidin-3-yl-methyl)]-amide;
- 10 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-
3-(3-methoxy-propyl-oxy)-phenyl]-octanoic acid [N-(3-carbamoyl-
3,3-dimethyl-propyl)]-amide;
- 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-
3-(4-methoxy-butyl)phenyl]-octanoic acid [N-(5(S)-2-
15 pyrrolidinon-5-yl-methyl)]-amide;
- 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-
3-(4-methoxy-butyl)-phenyl]-octanoic acid [N-(5(R)-2-
pyrrolidinon-5-yl-methyl)]-amide;
- 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-
20 3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(6(S)-2-oxo-
piperidin-6-yl-methyl)]-amide;
- 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-
3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(6(R)-2-oxo-
piperidin-6-yl-methyl)]-amide;
- 25 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-
3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(2-thiazol-2-
yl-ethyl)]-amide;
- 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-
30 3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(4(S)-2-
oxazolidinon-4-yl-methyl)]-amide;
- 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-
3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(4(R)-2-
oxazolidinon-4-yl-methyl)]-amide;

- 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-
3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (3 (S) -2.5-
dioxo-pyrrolidin-3-yl-methyl)] -amide;
- 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-
5 3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (3 (R) -2.5-
dioxo-pyrrolidin-3-yl-methyl)] -amide;
- 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-
3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (2,6-dioxo-
10 piperidin-4-yl-methyl)] -amide;
- 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-
3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (4 (S) -2-
oxothiazolidin-4-yl-methyl)] -amide;
- 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-
3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (4 (R) -2-
15 oxothiazolidin-4-yl-methyl)] -amide;
- 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-
3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (tetrahydro-2-
pyrimidon-5-yl-methyl)] -amide;
- 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-
20 3- (3-methoxypropyloxy) -phenyl] -octanoic acid [N- (N-acetyl-2-
amino-2-methyl-propyl)] -amide;
- 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-
3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (N-formyl-2-
amino-2-methyl-propyl)] -amide;
- 25 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-
3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (4-acetyl-
piperazinyl-ethyl)] -amide;
- 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-
3- (3-methoxy-propyloxy) -phenyl] -octanoic acid [N- (2,4-
30 imidazolinedion-5-yl-methyl)] -amide;
- 5 (S) -amino-4 (S) -hydroxy-2 (S) , 7 (S) -diisopropyl-8- [4-methoxy-
3- (4-methoxy-butyl) phenyl] -octanoic acid [N- (2-hydroxy-pyridin-
6-yl-methyl)] -amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(2,2-dimethyl-2-sulfamoyl-ethyl)]-amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(2,2-dimethyl-2-(N,N-dimethyl)-sulfamoyl-ethyl)]-amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(2-oxo-piperidin-3 (R)-yl)]-amide;

10 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(2-oxo-piperidin-3 (S)-yl)]-amide;

15 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(2-oxo-piperidin-4-yl)]-amide;

5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxy-propyloxy)-phenyl]-octanoic acid [N-(N-acetyl-piperidin-4-yl)]-amide; or

20 5 (S)-amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(4-methoxy-but-1-en-yl)-phenyl]-octanoic acid [N-(2-carbamoyl-2,2-dimethyl-ethyl)]-amide; and pharmaceutically acceptable salts thereof.

25 8. A method according to claim 1 wherein the compound is 5 (S)-Amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxypropyloxy)-phenyl]-octanoic acid morpholinopropyl)amide or a pharmaceutically acceptable salt thereof.

30 9. A method according to claim 1 wherein the compound is 5 (S)-Amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxypropyloxy)-phenyl]-octanoic acid morpholinoethyl)amide or a pharmaceutically acceptable salt thereof.

10. A method according to claim 1 wherein the compound is
5 (S)-Amino-4(S)-hydroxy-2(S), 7(S)-diisopropyl-8-[4-methoxy-3-(3-methoxypropyloxy)-phenyl]-octanoic acid {N-[2-(N-methylcarbamoyl)-1(R,S)-methyl-ethyl]}-amide or a pharmaceutically acceptable salt thereof.

11. A method according to claim 1 wherein the compound is
5 (S)-Amino-4(S)-hydroxy-2(S), 7(S)-diisopropyl-8-[4-methoxy-3-(3-methoxypropyloxy)-phenyl]-octanoic acid N-(3-carbamoylpropyl)amide or a pharmaceutically acceptable salt thereof.

12. A method according to claim 1 wherein the compound is
5 (S)-Amino-4(S)-hydroxy-2(S), 7(S)-diisopropyl-8-[4-methoxy-3-(3-methoxypropyloxy)-phenyl]-octanoic acid {N-[2(R)-(N-methylcarbamoyl)-2(R)-methyl-ethyl]}-amide or a pharmaceutically acceptable salt thereof.

13. A method according to claim 1 wherein the compound is
5 (S)-Amino-4(S)-hydroxy-2(S), 7(S)-diisopropyl-8-[4-methoxy-3-(3-methoxypropyloxy)-phenyl]-octanoic acid N-(2-thiomorpholinoethyl)amide or a pharmaceutically acceptable salt thereof.

25 14. A method according to claim 1 wherein the compound is
5 (S)-Amino-4(S)-hydroxy-2(S), 7(S)-diisopropyl-8-[4-methoxy-3-(3-methoxypropyloxy)-phenyl]-octanoic acid N-[2-(N,N-dimethylcarbamoyl)ethyl]amide or a pharmaceutically acceptable salt thereof.

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15. A method according to claim 1 wherein the compound is
5 (S)-Amino-4(S)-hydroxy-2(S), 7(S)-diisopropyl-8-[4-methoxy-3-(3-methoxypropyloxy)-phenyl]-octanoic acid N-(2-carbamoyl-1(R,S)-

methyl-ethyl)amide or a pharmaceutically acceptable salt thereof.

16. A method according to claim 1 wherein the compound is
5 (S)-Amino-4(S)-hydroxy-2(S),7(S)-diisopropyl-8-[4-methoxy-3-(3-methoxypropyloxy)-phenyl]-octanoic acid N-[2(R)-carbamoyl-2(R)-methyl-ethyl]-amide or a pharmaceutically acceptable salt thereof.

10 17. A method according to claim 1 wherein the compound is
5 (S)-Amino-4(S)-hydroxy-2(S),7(S)-diisopropyl-8-[4-methoxy-3-(3-methoxypropyloxy)-phenyl]-octanoic acid N-(2-carbamoyl-2,2-dimethyl-ethyl)amide or a pharmaceutically acceptable salt thereof.

15 18. A method according to claim 1 wherein the compound is
5 (S)-Amino-4(S)-hydroxy-2(S),7(S)-diisopropyl-8-[4-methoxy-3-(3-methoxypropyloxy)-phenyl]-octanoic acid N-[2-(N-acetyl)-piperidin-4-yl]ethyl]amide or a pharmaceutically acceptable salt
20 thereof.

19. A method according to claim 1 wherein the compound is
5 (S)-Amino-4(S)-hydroxy-2(S),7(S)-diisopropyl-8-[4-methoxy-3-(3-methoxypropyloxy)-phenyl]-octanoic acid {N-[(N,N-dimethyl)-25 carbamoyl-methyl]}-amide or a pharmaceutically acceptable salt thereof.

20. A method according to claim 1 wherein the compound is
5 (S)-Amino-4(S)-hydroxy-2(S),7(S)-diisopropyl-8-[4-methoxy-3-(3-methoxypropyloxy)-phenyl]-octanoic acid N-[2(R,S)-(N-methylcarbamoyl)-2(R,S)-methyl-ethyl]-amide or a
30 pharmaceutically acceptable salt thereof.

21. A method according to claim 1 wherein the compound is 5 (S)-Amino-4 (S)-hydroxy-2 (S), 7 (S)-diisopropyl-8-[4-methoxy-3-(3-methoxypropoxy)-phenyl]-octanoic acid N-(2-carbamoyl-2,2-dimethyl-ethyl)-amide or a pharmaceutically acceptable salt thereof.

22. A method according to claim 1 wherein the compound is 5 (S)-Amino-2 (S), 7 (S)-diisopropyl-4 (S)-hydroxy-8-[4-tert-butyl-3-(3-methoxypropoxy)-phenyl]-octanoic acid [N-2-(morpholin-4-yl)-ethyl]-amide or a pharmaceutically acceptable salt thereof.

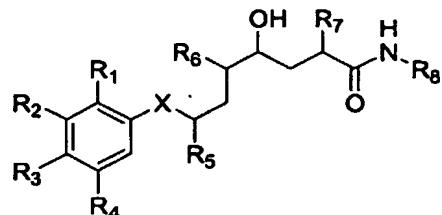
23. A method according to claim 1, wherein the subject is a human.

15 24. A method according to claim 1, wherein the disease is dementia.

25 25. A method according to claim 1, wherein the disease is Alzheimer's disease.

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26. A method for making a compound of the formula



wherein

R₁ is hydrogen, hydroxy, lower alkoxy, cycloalkoxy, lower alkoxy-lower alkoxy or free or esterified or amidated carboxy-lower alkoxy;

R₂ is hydrogen, lower alkyl, cycloalkyl, lower alkoxy-lower alkyl, lower alkoxy-lower alkoxy-lower alkyl, cycloalkoxy-lower alkyl, hydroxy, optionally lower alkanoylated,

halogenated or sulfonylated hydroxy-lower alkoxy; amino-lower alkyl that is unsubstituted or substituted by lower alkyl, by lower alkanoyl and/or by lower alkoxycarbonyl; optionally hydrogenated heteroaryl-lower alkyl; amino-lower alkoxy that is substituted by lower alkyl, by lower alkanoyl and/or by lower alkoxycarbonyl; oxo-lower alkoxy, lower alkoxy, cycloalkoxy, lower alkenyloxy, cycloalkoxy-lower alkoxy, lower alkoxy-lower alkoxy, lower alkoxy-lower alkenyl, lower alkenyloxy-lower alkoxy, lower alkoxy-lower alkenyloxy, lower alkenyloxy-lower alkyl, lower alkanoyl-lower alkoxy, optionally S-oxidised lower alkylthio-lower alkoxy, lower alkylthio-(hydroxy)-lower alkoxy, aryl-lower alkoxy, optionally hydrogenated heteroaryl-lower alkoxy, cyano-lower alkoxy, free or esterified or amidated carboxy-lower alkoxy or free or esterified or amidated carboxy-lower alkyl;

R₃ is halogenated lower alkyl, lower alkoxy-lower alkyl, cycloalkoxy-lower alkyl, hydroxy-lower alkyl, optionally S-oxidised lower alkylthio-lower alkyl, optionally hydrogenated heteroarylthio-lower alkyl; amino-lower alkyl that is unsubstituted or N-mono- or N,N-di-lower alkylated. N-lower alkanoylated or N-lower alkane-sulfonylated or N,N-disubstituted by lower alkylene, by unsubstituted or N'-lower alkylated or N'-lower alkanoylated aza-lower alkylene, by oxa-lower alkylene or by optionally S-oxidised thia-lower alkylene; cyano-lower alkyl, free or esterified or amidated carboxy-lower alkyl, cycloalkyl, aryl, hydroxy, lower alkoxy, cycloalkoxy, lower alkoxy-lower alkoxy, cycloalkoxy-lower alkoxy, hydroxy-lower alkoxy, aryl-lower alkoxy, optionally halogenated lower alkoxy, optionally S-oxidised lower alkylthio-lower alkoxy, optionally hydrogenated heteroaryl-lower alkoxy, optionally

hydrogenated heteroarylthio-lower alkoxy; amino-lower alkoxy that is unsubstituted or N-mono- or N,N-di-lower alkylated. N-lower alkanoylated or N-lower alkanesulfonylated or substituted by lower alkylene, by unsubstituted or N'-lower alkylated or N'-lower alkanoylated aza-lower alkylene, by oxa-lower alkylene or by optionally S-oxidised thia-lower alkylene; cyano-lower alkoxy or free or esterified or amidated carboxy-lower alkoxy;

10 R₄ is hydrogen, lower alkyl, hydroxy, lower alkoxy or cycloalkoxy;

X is methylene;

R₅ is lower alkyl or cycloalkyl;

15 R₆ is unsubstituted or N-mono- or N,N-di-lower alkylated or N-lower alkanoylated amino;

R₇ is lower alkyl, lower alkenyl, cycloalkyl or aryl-lower alkyl; and

20 R₈ is lower alkyl, cycloalkyl, free or aliphatically esterified or etherified hydroxy-lower alkyl; amino-lower alkyl that is unsubstituted or N-lower alkanoylated or N-mono- or N,N-di-lower alkylated or N,N-disubstituted by lower alkylene, by hydroxy- lower alkoxy- or lower alkanoyloxy-lower alkylene, by unsubstituted or N'-lower alkanoylated or N'-lower alkylated aza-lower alkylene, by oxa-lower alkylene or by optionally S-oxidised thia-lower alkylene; free or esterified or amidated carboxy-lower alkyl, free or esterified or amidated dicarboxy-lower alkyl, free or esterified or amidated carboxy-(hydroxy)-lower alkyl, free or esterified or amidated carboxycycloalkyl-lower alkyl,

25 cyano-lower alkyl, lower alkanesulfonyl-lower alkyl, unsubstituted or N-mono- or N,N-di-lower alkylated thiocarbamoyl-lower alkyl, unsubstituted or N-mono- or N,N-di-lower alkylated sulfamoyl-lower alkyl, or a heteroaryl

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radical bonded via a carbon atom and optionally hydrogenated and/or oxo-substituted, or lower alkyl substituted by a heteroaryl radical bonded via a carbon atom and optionally hydrogenated and/or oxo-substituted, or a pharmaceutically acceptable salt thereof.

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